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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/579,622	05/16/2006	Susanne Moira Brown	69477575701	9395
24197 7590 04/24/2007 KLARQUIST SPARKMAN, LLP 121 SW SALMON STREET SUITE 1600 PORTLAND, OR 97204			EXAMINER SHIN, DANA H	
			ART UNIT 1635	PAPER NUMBER
SHORTENED STATUTORY PERIOD OF RESPONSE		MAIL DATE	DELIVERY MODE	
3 MONTHS		04/24/2007	PAPER	

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/579,622	BROWN ET AL.	
	Examiner	Art Unit	
	Dana Shin	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 March 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-28,33-36,42,44,45,47-74,76-79 and 86-94 is/are pending in the application.
- 4a) Of the above claim(s) 48-74,76-79,86-89,92 and 93 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-28,33-36,42,44,45,47,90,91 and 94 is/are rejected.
- 7) ☒ Claim(s) 4,5 and 7 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 7-13-06.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of claims 1-29, 33-36, 42, 44-45, 47, 90-91 as well as SEQ ID NO:1 in the reply filed on March 15, 2007 is acknowledged. The traversal is on the ground(s) that the special technical feature has been mischaracterized. This is not found persuasive because of the following reasons:

1) The first recited claim (claim 1) and its dependent claims, as originally presented, recite the herpes simplex virus comprising a nucleic acid encoding an antisense to SCCRO (comprising either SEQ ID NO:1 or 3), while the claims that are separately grouped recite the herpes simplex virus comprising a nucleic acid encoding siRNA molecule capable of repressing SCCRO (comprising SEQ ID NO:5). Hence, the instant application on its face does not contain a single technical relationship between the groups or the same special technical features shared by the two groups under PCT Rule 13.1, but rather contains two special technical features that are divergent and independent for the reasons stated in the previous Office action. Note that PCT Rule 13.1 states "The international application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept.

2) Applicant argues that the International Search Authority found a single inventive concept by examining all claims. Contrary to applicant's assertions, the different inventions of the instant application, according to domestic (U.S.) restriction practice under 35 U.S.C. 121 and 372 (see page 2 of the previous Office action), comprise functionally, chemically, and biologically distinct compositions and methods, and thus comprise patentably distinct inventions.

Further, the special technical features of the presently claimed inventions do not make a contribution over the prior art under PCT Rules 13.1. and 13.2. See §103 rejections below. Accordingly, the inventions claimed in the instant case are not linked as to form a single general inventive concept.

3) With regard to the sequence restriction requirement, the field of search for SEQ ID NO:1 and SEQ ID NO:3 is considered co-extensive due to significant homology between the two nucleic acid sequences as applicant claims. Accordingly, both SEQ ID NOs: 1 and 3 will be examined in the instant case.

The requirement is still deemed proper and is therefore made FINAL.

Status of Claims

Claims 48-74, 76-79, 86-89, and 92-93 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Accordingly, claims 1-28, 33-36, 42, 44-45, 47-74, 76-79, and 86-94 are pending, and claims 1-28, 33-36, 42, 44-45, 47, 90-91, and 94 are currently under examination on the merits.

Oath/Declaration

The declaration lacks the statement of venue. Applicant is required to furnish either a new oath or declaration in proper form, identifying the application by application number and filing date. The current declaration identifies PCT/GB2004/004908, not the present application. The new oath or declaration must properly identify the application of which it is to form a part,

Art Unit: 1635

preferably by application number and filing date in the body of the oath or declaration. See MPEP §§ 602.01 and 602.02.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. See page 34. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Objections

Claims 4-5 and 7 are objected to because of the following informalities:

- 1) Claims 4 and 5, line 6 recites “(iii) to a fragment of said polynucleotide sequence”. It appears that “to” is repetitive and should be omitted.
- 2) Claim 7, lines 1-2 recite “wherein a said fragment comprises”. The article “a” should be omitted. Appropriate correction is required.

Claim Rejections - 35 USC § 112, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-28, 33-36, 42, 44-45, 90-91, and 94 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably

Art Unit: 1635

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and /or chemical properties, functional characteristics, structure/function correlation, or any combination thereof.

The claims are drawn to a herpes simplex virus encoding an antisense to the squamous cell carcinoma related oncogene (asSCCRO), a method of killing tumor cells *in vivo* comprising administering the herpes simplex virus comprising asSCCRO to a patient in need of treatment and a medicament or pharmaceutical composition comprising the herpes simplex virus comprising asSCCRO. As such, the instant claims embrace constructs having any species of herpes simplex virus comprising any species of antisense nucleic acids to the squamous cell carcinoma related oncogene. The instant specification discloses only a single species of herpes simplex virus comprising asSCCRO, known as ECACC accession number 04051901 in the instant case, which is shown to be capable of killing tumor cells. This single exemplified species is not a representative number of species of the broadly claimed genus of the herpes simplex virus encoding asSCCRO.

Note that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species. A “representative number of species” means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. The disclosure of only one species

Art Unit: 1635

encompassed within a genus adequately describes a claim directed to that genus only if the disclosure "indicates that the patentee has invented species sufficient to constitute the gen[us]." See *Enzo Biochem*, 323 F.3d at 966, 63 USPQ2d at 1615; *Noelle v. Lederman*, 355 F.3d 1343, 1350, 69 USPQ2d 1508, 1514 (Fed. Cir. 2004) (Fed. Cir. 2004)("[A] patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated."). See also MPEP §2163.

In light of the above, the instant specification does not clearly allow persons of ordinary skill in the art to recognize that the inventors invented the genus claimed in the instant case. See *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1562, 19 USPQ2d 1111, 1115 (Fed. Cir. 1991), which clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (see page 1117).

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 6 recites the limitation "said degree of sequence identity" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim.

Regarding claim 7, the length limitation recited in line 2, "fragment comprises at least 20 nucleotides and no more than 900 nucleotides" is internally inconsistent with SEQ ID NO:3 claimed in claim 4. As written, the fragment of SEQ ID NO:3 should comprise up to 900 nucleotides; however, the entire length of SEQ ID NO:3 is only 876 nucleotides. Therefore, it is unclear how a fragment of a polynucleotide comprising a total of 876 nucleotides can comprise up to 900 nucleotides, thus rendering the claim indefinite.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Art Unit: 1635

Claims 1-28, 33, 36, 47, and 94 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nemunaitis (*Biodrugs*, 2003, 17:251-262) in view of Tang et al. (US 2003/0022329 A1) and Jacobs et al. (*Human Gene Therapy*, 2003, 14:277-297).

The claims are drawn to a herpes simplex virus comprising an antisense nucleic acid to the squamous cell carcinoma related oncogene (SCCRO) that is mammalian and human and have at least 60% identical or 70% identical and is complementary to SEQ ID NO:1 or 3 or complementary to or hybridizes to a fragment of SEQ ID NO:1 or 3, wherein said fragment comprises 20 to 900 nucleotides, said nucleic acid is located in at least one RL1 locus, at least one of the ICP34.5 protein coding sequences, wherein the simplex virus is a mutant of HSV-1 strain 17, a gene specific null mutant, an ICP34.5 null mutant, lacks one expressible ICP34.5 gene, non-neurovirulent, and a herpes simplex virus comprising a regulatory sequence operably linked to the antisense nucleic acid or a herpes simplex virus antisense cassette comprising asSCCRO, a ribosome binding site (IRES), and a marker (GFP), wherein the transcript product is a bi- or poly- cistronic transcript, wherein the herpes simplex virus is HSV1716asSCCRO, and further comprising a polyadenylation sequence (SV40), a method of killing tumor cells *in vitro* comprising administering herpes simplex virus comprising asSCCRO,

The reference of Nemunaitis teaches that selective replicating viral vectors show tumor-selective replication. It teaches that anti-tumor effect is observed in animal models as well as patients with cancer without evidence of significant toxicity when viral vectors such as herpes simplex virus are used alone or as gene delivery vehicles. It teaches that modifications may enable more aggressive use of the viral vectors as systemic gene delivery vehicles. It teaches that selective replication DNA viruses can be engineered to carry and deliver cancer-toxic genes. See

Art Unit: 1635

pages 251-252. It teaches that HSV mutants lacking ICP34.5 have been shown to be effective in treatment of tumors, both CNS and non-CNS, in animal models (page 255). It teaches that HSV mutant viruses are reasonable gene delivery vectors for future cancer therapeutic investigation. See page 256. The reference of Nemunaitis does not teach inserting asSCCRO sequence into HSV mutant virus or the HSV mutant virus comprises IRES, GFP, and SV40, producing bi- or poly-cistronic transcript.

Tang et al. teach SEQ ID NO:22, which is 94.9% identical to the nucleic acid sequence of instant SEQ ID NO:1. They teach that SEQ ID NO:22 can be used as an antisense polynucleotide molecule (paragraph 0007). They teach that antisense therapy or gene therapy can be applied to downregulate the expression of the expression of polypeptides encoded by SEQ ID NO:22 (paragraphs 0120-0121, 0238). They further teach that the antisense molecule comprising SEQ ID NO:22 can be used to inhibit squamous cell carcinoma (paragraph 0195). They teach that the vector carrying a polynucleotide sequence comprises one or more phenotypic selectable markers and the selection of the appropriate vector and promoter is well within the level of ordinary skill in the art (paragraph 0088). They teach that the regulatory sequences of the endogenous gene may be replaced with the polynucleotides by homologous recombination, which is one of routine genetic engineering methods in the art (paragraph 0097).

Jacobs et al. teach cloning of various genetically engineered herpes simplex virus amplicon vectors comprising GFP, IRES, therapeutic gene sequence, and SV40 polyadenylation signal sequence through series of digestion and ligation steps (page 279 and Figure 1). They teach generation of IRES-based double-gene co-expression cassettes and triple-gene co-expression cassettes (pages 279-281). They teach that the genetically engineered herpes simplex

Art Unit: 1635

virus amplicon vectors show IRES-mediated reduction of expression of the gene in cells (pages 284-286). They teach that the herpes simplex virus vectors comprising IRES, GFP, therapeutic gene sequence, and SV40 poly A sequence can be used to monitor the level and distribution of vector-mediated gene expression *in vivo*, which therefore can be used in clinical gene therapy applications (pages 294-295).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to insert the antisense polynucleotide of Tang et al. into the HSV mutant of Nemunaitis through recombination technology of Johns et al. One of ordinary skill in the art would have been motivated to use the HSV mutant lacking ICP34.5 of Nemunaitis to express the therapeutic antisense polynucleotide of Tang et al. with a reasonable expectation of success, because the HSV mutant lacking ICP34.5 had previously been shown to be effective in treating both CNS and non-CNS tumors in animal models and therefore suggested to be effective as a gene delivery vector for future cancer therapeutic investigation by Nemunaitis (pages 255-256), and because Tang et al. taught that the antisense polynucleotide comprising SEQ ID NO:22 can be used to inhibit squamous cell carcinoma. Further, the skilled artisan would have been motivated to genetically alter the HSV mutants lacking ICP34.5 to comprise GFP, IRES, therapeutic gene sequence, and SV40 polyadenylation signal sequence through series of digestion and ligation steps or through routine homologous recombination techniques as taught by Tang et al. and Jacobs et al., because such HSV vectors are useful for monitoring the level and distribution of vector-mediated gene expression *in vivo*, which therefore can be used in clinical gene therapy applications as taught by Jacobs et al. (pages 294-295). Accordingly, the

Art Unit: 1635

instantly claimed invention taken as a whole would have been *prima facie* obvious at the time of filing.

Claims 1-3, 9-18, 33-36, 42, 44, 45, 90-91 and 94 are rejected under 35 U.S.C. 103(a) as being unpatentable over Coukos et al. (*Clinical Cancer Research*, 1999, 5:1523-1537) in view of Sidransky (US 6,025,127) and Glorioso et al. (WO 98/51809, applicant's citation, IDS filed on July 13, 2006).

The claims are described above.

Coukos et al. teach that HSV-1 mutants replicate preferentially in tumor cells, resulting in a direct oncolytic effect but sparing normal differentiated tissues (pages 1523-1524). They teach that a particular HSV-1 mutant, namely HSV-1716, is effective in not only safely reducing tumor volume in mice but also prolonging survival of tumor-bearing mice (pages 1524-1533). They teach that HSV-1716 lacks ICP34.5 (pages 1523-1524). They teach that ICP34.5 null HSV-1 mutants replicate preferentially in tumor cells and have been successfully used to reduce or cure tumors of the central nervous system in experimental models, indicating that ICP34.5 null HSV-1 mutants are non-neurovirulent (page 1524). They teach that HSV-1 mutants can be used as gene therapy vectors with significant advantages over replication-incompetent adenoviral or retroviral vectors (page 1535). In particular, they teach that HSV-1 mutant strains are being engineered with progressively increased specificity and the insertion of corrective genes may further increase the efficacy of the oncolytic effect of the HSV-1 mutants (page 1535).

The Sidransky patent teaches methods for detecting target neoplastic nucleic acids and antisense oligonucleotides specific for target proto-oncogenic nucleic acids associated with head

Art Unit: 1635

and neck squamous carcinoma (columns 1-2). It teaches that antisense therapy comprising antisense nucleic acid molecules that are complementary to at least a portion of a specific mRNA molecule can be used to block production of neoplastic cells (columns 12-13). It teaches that various viral vectors that can be utilized for gene therapy including herpes virus can be used to deliver antisense proto-oncogene polynucleotides (columns 14-15).

Glorioso et al. teach that a mutant HSV virus can be engineered by inserting a pharmacologically active therapeutic polynucleotide within the HSV genome via homologous recombination procedure (pages 3-5; Figures 1-2). They teach that the polynucleotide is a synthetic DNA, cDNA, genomic DNA fragment, biologically active antisense RNA, or ribozyme (page 15). They teach that a mutant HSV vector contains a polynucleotide for expression in place of a native HSV locus (pages 17-18).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to replace the ICP34.5 locus with the antisense sequence targeted to the head and neck squamous carcinoma gene via homologous recombination procedure. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success because Glorioso et al. teach that a mutant HSV virus can be engineered by inserting a pharmacologically active therapeutic polynucleotide within the HSV genome by replacing a native HSV locus with an antisense polynucleotide via homologous recombination procedure. In light of the teachings of Glorioso et al., the skilled artisan would have been motivated to replace the ICP34.5 locus of HSV genome with the antisense sequence targeted to the head and neck squamous carcinoma gene with a reasonable expectation of success, because Coukos et al. teach that ICP34.5 null HSV-1 mutants replicate preferentially in tumor cells and have been successfully used to reduce

Art Unit: 1635

or cure tumors of the central nervous system in experimental models and therefore can be used as gene therapy vectors with significant advantages (pages 1523-1525), and because Sidransky teaches that herpes virus can be used to deliver antisense proto-oncogene polynucleotides, one of which is the antisense polynucleotide to the head and neck squamous carcinoma gene (columns 1-2, 14-15). Accordingly, the instantly claimed invention taken as a whole would have been *prima facie* obvious at the time of filing.

Claims 1-28, 33-36, 42, 44-45, 47, 90-91, and 94 are rejected under 35 U.S.C. 103(a) as being unpatentable over Toyozumi et al. (*Human Gene Therapy*, 1999, 10:3013-3029) in view of Estilo et al. (*Clinical Cancer Research*, 2003, 9:2300-2306, applicant's citation, IDS filed on July 13, 2006) and Jacobs et al. (*Human Gene Therapy*, 2003, 14:277-297).

The claims are described above.

Toyozumi et al. teach that the side effect profiles in the dose escalation phase I clinical trials using the ICP34.5 deletion mutant HSV-1716, or the ICP34.5- and RR-deleted HSV-1 mutant G207, for the treatment of malignant glioma are reported to be minimal, and thus both HSV-1716 and HSV-G207 are promising therapeutic agents for cancer therapy (page 3014). They teach that the oncolytic effect of HSV-R3616, lacking both copies of the ICP34.5 gene, is reported to be increased by coexpression of interleukin 4 in the treatment of malignant glioma. Further, HSV-G207 carrying IL-12 gene shows increased oncolytic effect in an experimental colon cancer model, and an HSV vector carrying IL-2 shows therapeutic efficacy in treating gastric carcinoma in mice (page 3014). They teach that combining HSV-1 mutant with another

chemotherapeutic agent is advantageous because a combination of agents with different toxicological profiles may result in increased efficacy through synergism (page 3015).

Estilo et al. teach that SCCRO is a significant predictor of tumor metastasis and therefore has a potential for antitumor therapeutics. They teach that the expression level of SCCRO is significantly greater in malignant tissues of head and neck squamous cell carcinoma (page 2300). They teach that the SCCRO-transfected cells form invasive tumor and develop regional lymph node metastasis in nude mice (page 2301). They teach that SCCRO mRNA expression correlates with established clinical and pathological indication of metastasis of squamous cell carcinoma (pages 2301-2304).

Jacobs et al. teach cloning of various genetically engineered herpes simplex virus amplicon vectors comprising GFP, IRES, therapeutic gene sequence, and SV40 polyadenylation signal sequence through series of digestion and ligation steps (page 279 and Figure 1). They teach generation of IRES-based double-gene co-expression cassettes and triple-gene co-expression cassettes (pages 279-281). They teach that the genetically engineered herpes simplex virus amplicon vectors show IRES-mediated reduction of expression of the gene in cells (pages 284-286). They teach that the herpes simplex virus vectors comprising IRES, GFP, therapeutic gene sequence, and SV40 poly A sequence can be used to monitor the level and distribution of vector-mediated gene expression *in vivo*, which therefore can be used in clinical gene therapy applications (pages 294-295).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use any one of ICP34.5 deletion mutant HSV-1716, ICP34.5-deleted HSV-1 mutant G207, HSV-R3616, and RR-deleted HSV-1 mutant G207 of Toyoizumi et al. to construct the

Art Unit: 1635

instantly claimed HSV mutant comprising asSCCRO. One of ordinary skill in the art would have been motivated to use any one of disclosed HSV mutants of Toyoizumi et al. as an expression vector to carry an antisense sequence to squamous cell carcinoma, with a reasonable expectation of success, because Toyoizumi et al. teach that HSV-G207 carrying IL-12 gene or IL-2 shows increased oncolytic effect and therapeutic efficacy in treating carcinoma and that combining HSV-1 mutant with another chemotherapeutic agent results in increased efficacy through synergism (pages 3014-3015), and because Estilo et al. teach that SCCRO mRNA expression correlates with metastasis of squamous cell carcinoma and therefore SCCRO is a potential for antitumor therapeutics (pages 2301-2304). Further, the skilled artisan would have been motivated to clone genetically engineered HSV mutant vectors comprising GFP, IRES, SV40 polyadenylation sequence as taught by Jacobs et al. by modifying any one of HSV mutants of Toyoizumi et al., and by inserting an antisense polynucleotide sequence of SCCRO of Estilo et al., because Jacobs et al. teach that genetically engineered HSV vectors comprising GFP, IRES, SV40 polyadenylation sequence, and a therapeutic gene sequence show IRES-mediated reduction of expression of the gene in cells and can be used to monitor the level and distribution of vector-mediated gene expression *in vivo*, which therefore can be used in clinical gene therapy applications (pages 284-286, 294-295). Accordingly, the instantly claimed invention taken as a whole would have been *prima facie* obvious at the time of filing.

Conclusion

No claim is allowed.

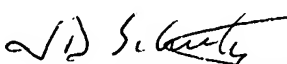
Art Unit: 1635

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dana Shin whose telephone number is 571-272-8008. The examiner can normally be reached on Monday through Friday, from 8am-4:30pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Douglas Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Dana Shin
Examiner
Art Unit 1635


J. DOUGLAS SCHULTZ, PH.D.
SUPERVISORY PATENT EXAMINER